90th General Session
World Organisation for Animal Health
World Assembly
Paris, 21-25 May 2023

Original: English

Activities of the Specialist Commissions

BIOLOGICAL STANDARDS COMMISSION

Proposed amendments to the
Manual of Diagnostic Tests and Vaccines
for Terrestrial Animals

(90 SG/10SC2)

TABLE OF CONTENTS

1. OVERVIEW OF TECHNICAL ACTIVITIES 3

1.1. Introduction 3

2. TERRESTRIAL MANUAL TEXTS THAT WILL BE PROPOSED FOR ADOPTION 3

2.1. Glossary of terms 3

2.2. Chapter 1.1.6. Principles and methods of validation of diagnostic assays for infectious diseases 3

2.3. Chapter 1.1.10. Vaccine banks 4

2.4. Chapter 3.1.1 Anthrax 4

2.5. Chapter 3.1.5. Crimean–Congo haemorrhagic fever 4

2.6. Chapter 3.1.18. Rabies (infection with rabies virus and other lyssaviruses) 4

2.7. Chapter 3.1.19. Rift Valley fever (infection with Rift Valley fever virus) 5

2.8. Chapter 3.1.22. Trichinellosis (infection with *Trichinella* spp.) 5

2.9. Chapter 3.2.2. American foulbrood of honey bees (infection of honey bees with Paenibacillus larvae) 5

2.10. Chapter 3.2.3. European foulbrood of honey bees (infection of honey bees with Melissococcus plutonius) 6

2.11. Chapter 3.3.10. Fowlpox 6

2.12. Chapter 3.3.13. Marek's disease 6

2.13. Chapter 3.4.12. Lumpy skin disease (Diagnostic techniques section only) 7

2.14. Chapter 3.7.2. Rabbit haemorrhagic disease 7

2.15. Chapter 3.9.7. Influenza A virus of swine 7

2.16. Chapter 3.10.1. Bunyaviral diseases of animals (excluding RVF fever and Crimean–Congo haemorrhagic fever) 7

******

1. OVERVIEW OF TECHNICAL ACTIVITIES

1.1. INTRODUCTION

Since the 89th General Session in May 2022, the Biological Standards Commission met twice, from 5 to 9 September 2022 and from 6 to 10 February 2023. Among its activities, the Commission progressed its work on the development of new and revised texts for the *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (*Terrestrial Manual*) in accordance with its work programme. Details of the Commission's activities, including links to the texts circulated for comment, were published in the Commission's September 2022 and February 2023 meeting reports and are available on the Delegate's only website as well as the WOAH Website.

This report provides a brief summary of each of the revised texts of the *Terrestrial Manual* that will be presented for adoption at the 90th General Session. Details of the Commission's consideration of comments received on draft texts circulated for comment, were provided in the Commission's September 2022 and February 2023 meeting reports. The Commission encourages Members to refer to these meeting reports for more details about the amended texts being proposed for adoption.

This document describes the proposed amendments to the chapters from the *Terrestrial Manual* that will be presented to the World Assembly of Delegates for adoption at the 90th General Session. A link to the revised *Terrestrial Manual* chapters is included on page 1 of the report of the February meeting of the Biological Standards Commission.

In the process of drafting and reviewing these amendments, the Commission considered comments submitted by Members and by International Organisations that have a cooperation agreement with WOAH.

2. TERRESTRIAL MANUAL TEXTS THAT WILL BE PROPOSED FOR ADOPTION

2.1. GLOSSARY OF TERMS

Two definitions are proposed: one for robustness as the term is used in the updated chapter 1.1.6 on validation of diagnostic assays, and one for anthroponosis in response to a Member comment on Chapter 3.9.7 *Influenza A virus of swine*.

A link to the definitions is included on page 1 of the reports of the meetings of the Biological Standards Commission. The definitions are to be proposed for adoption at the 90th General Session in May 2023.

2.2. CHAPTER 1.1.6. PRINCIPLES AND METHODS OF VALIDATION OF DIAGNOSTIC ASSAYS FOR INFECTIOUS DISEASES

Chapter 1.1.6. *Principles and methods of validation of diagnostic assays for infectious diseases* has undergone a comprehensive revision. The revised text was first circulated for comment in October 2022. The main amendments include: added reference to point-of-care tests (POCTs) and virtual biobanks given their increasing use and importance; improved presentation of criteria for assay development and validation; added a table highlighting test purposes and relative importance of different performance parameters; updated Figure 1 to include extra field validation step for POCTs; included a summary table on challenges and opportunities for diagnostic test validation; added new sections on new technologies and conclusions.

A link to the revised Chapter 1.1.6. *Principles and methods of validation of diagnostic assays for infectious diseases* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.3. CHAPTER 1.1.10. VACCINE BANKS

Chapter 1.1.10. *Vaccines banks* has undergone a comprehensive revision. The revised text was first circulated for comment in October 2022. The main amendments include: updated the definition of a vaccine bank; revised the section on types of banks stressing the need for compliance with the principles of GMP[1]; thoroughly updated the sections on *Types of banks*, *Selection of vaccines for a bank*, *Regulatory considerations, Storage of vaccines or antigens in a bank* and *Deployment planning,* for example by expanding the information on DIVA[2] vaccines.

A link to the revised Chapter 1.1.10. *Vaccine banks* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.4. CHAPTER 3.1.1 ANTHRAX

Chapter 3.1.1. *Anthrax* has undergone a moderate revision. The revised text was first circulated for comment in October 2022. The main amendments include: updated the capsule visualisation (staining) method to include a new capsule stain that is quicker to make and thus more readily available and convenient, but kept the polychrome methylene blue (M'Fadyean reaction) stain as it is still in use; stressed the importance of avoiding environmental contamination by closing all natural orifices on carcasses of animals suspected to have died of anthrax, and emphasised that post-mortem examination is prohibited in many countries when anthrax is suspected; upgraded the rating of the PCR for the purpose *Confirmation of clinical cases* in Table 1 as the presence of toxin genes can be demonstrated directly.

A link to the revised Chapter 3.1.1. *Anthrax* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.5. CHAPTER 3.1.5. CRIMEAN–CONGO HAEMORRHAGIC FEVER

Chapter 3.1.5. *Crimean–Congo haemorrhagic fever* has undergone a moderate revision. The revised text was first circulated for comment in October 2022. The main amendments include: removed all mention of intracerebral inoculation of suckling mice for animal welfare reasons; in Table 1. amended the ratings of the tests for the purpose *Confirmation of clinical cases in animals* to align with the proposed case definition and added footnotes to clarify the diagnostic use of the tests; in the Section on *Nucleic acid detection* updated the classification of the virus clades and added a table of corresponding recommended primer sequences, which replaces the sequences and cycling parameters currently given for a real-time RT-PCR[3].

A link to the revised Chapter 3.1.5. *Crimean–Congo haemorrhagic fever* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.6. CHAPTER 3.1.18. RABIES (INFECTION WITH RABIES VIRUS AND OTHER LYSSAVIRUSES)

Chapter 3.1.18. *Rabies* (*infection with rabies virus and other lyssaviruses*) has undergone a moderate revision. The revised text was first circulated for comment in October 2022. The main amendments include: in Table 1 – deleted the antigen-detection ELISA[4], and changed "cell culture" to "RTCIT"[5] and amended its rating for the purpose "Population freedom from infection"; added a section on rapid immunochromatographic tests (lateral flow devices) but stressed the limitations of these tests, including their lack of sensitivity; added a paragraph to the vaccine section mentioning rabies virus glycoprotein biotechnology-derived vector vaccines and the possible future availability of non-replication-competent constructs or replication-restricted rabies vaccine constructs: the Commission supported including information on vaccines in the advanced

[1] GMP: Good Manufacturing Practice
[2] DIVA: differentiation of infected from vaccinated animals
[3] RT-PCR: reverse transcription PCR
[4] ELISA: enzyme-linked immunosorbent assay
[5] RTCIT: rabies tissue culture infection test

stages of development and potentially available in the future as it is important for Members to be aware of advances in vaccinology.

A link to the revised Chapter 3.1.18. *Rabies* (*infection with rabies virus and other lyssaviruses*) is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.7. CHAPTER 3.1.19. RIFT VALLEY FEVER (INFECTION WITH RIFT VALLEY FEVER VIRUS)

Chapter 3.1.19. *Rift Valley fever* (*infection with Rift Valley fever virus*) has undergone a moderate revision. The revised text was first circulated for comment in October 2022. The main amendments include: removed all mention of virus isolation in suckling mice for animal welfare reasons; updated the protocols for the agarose gel-based RT-PCR, the antigen ELISA, the plaque reduction neutralisation test, and added a pen-side rapid diagnostic test (lateral flow device), a blocking IgG ELISA and a virus neutralisation test; on the advice of the experts, upgraded the ratings of the RT-PCR and antigen detection in Table 1 for the purpose *Individual animal freedom from infection prior to movement*; in the vaccine section, added MP-12 attenuated virus vaccine to the table summarising the current RVF vaccine strains and to the text, and deleted TSI–GSD–200 inactivated human vaccine as it is presently not available.

A link to the revised Chapter 3.1.19. *Rift Valley fever* (*infection with Rift Valley fever virus*) is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.8. CHAPTER 3.1.22. TRICHINELLOSIS (INFECTION WITH *TRICHINELLA* SPP.)

Chapter 3.1.22. *Trichinellosis* (*infection with* Trichinella *spp*.) has undergone a comprehensive revision. The revised text was first circulated for comment in October 2022. The main amendments include: updated the taxonomy of the genus *Trichinella*; deleted antigen detection from Table 1 as it is not fit for any of the purposes, amended the rating of the PCR for the purpose *Prevalence of infection – surveillance* as species-level information is relevant for surveillance purposes, and added two footnotes to the Table to clarify which tests can be used in combination as confirmatory tests; updated the digestion and detection methods and added three new direct detection methods; deleted the section on Trichinoscopy as the method is not recommended.

A link to the revised Chapter 3.1.22. *Trichinellosis* (*infection with* Trichinella *spp*.) is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.9. CHAPTER 3.2.2. AMERICAN FOULBROOD OF HONEY BEES (INFECTION OF HONEY BEES WITH PAENIBACILLUS LARVAE)

Chapter 3.2.2. *American foulbrood of honey bees* (*infection of honey bees with* Paenibacillus larvae) has undergone a moderate revision. The revised text was first circulated for comment in October 2022. The main amendments include: updated the text throughout to take account of the new genotype (ERIC V) including adding it to Table 2. *Phenotypic characteristics of* Paenibacillus larvae *ERIC genotypes*; clarified that larvae infected with ERIC I usually die after brood cell capping, whereas larvae infected with other types usually die before cell caping; stressed that whole genome sequencing showed a good correlation with conventional typing methods and was used efficiently for cluster delineation in American foulbrood outbreak epidemiological investigations; added explanatory text on real-time PCRs.

A link to the revised Chapter 3.2.2. *American foulbrood of honey bees* (*infection of honey bees with* Paenibacillus larvae) is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.10. CHAPTER 3.2.3. EUROPEAN FOULBROOD OF HONEY BEES (INFECTION OF HONEY BEES WITH MELISSOCOCCUS PLUTONIUS)

Chapter 3.2.3. *European foulbrood of honey bees* (*infection of honey bees with* Melissococcus plutonius) has undergone a moderate revision. The revised text was first circulated for comment in October 2022. The main amendments include: added information on atypical strains; clarified that both disease signs and the presence of *M. plutonius* are required for diagnosis; thoroughly updated the section on *Epizootiology and clinical signs* including replacing Figure 1 on irregular capping of the brood with an improved photograph; updated the section on culture methods; added explanatory text on real-time PCRs; and mentioned that the current taxonomic position of *Achromobacter* eurydice remains uncertain.

A link to the revised Chapter 3.2.3. *European foulbrood of honey bees* (*infection of honey bees with* Melissococcus plutonius) is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.11. CHAPTER 3.3.10. FOWLPOX

Chapter 3.3.10. *Fowlpox* has undergone a moderate revision. The revised text was first circulated for comment in October 2022. The main amendments include: thoroughly updated Table 1*:* added [conventional] PCR and separated it from RT-PCR, added histopathology, replaced IFAT[6] with VN[7] added a new test – MIFI[8], and changed the rating of all the tests in the Table except AGID[9]; updated the molecular methods including the primer sequences; deleted passive haemagglutination, fluorescent antibody tests, immunoperoxidase and immunoblotting methods as they are no longer used; mentioned the availability of recombinant fowlpox vaccines

A link to the revised Chapter 3.3.10. *Fowlpox* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.12. CHAPTER 3.3.13. MAREK'S DISEASE

Chapter 3.3.13. *Marek's disease* has undergone a comprehensive revision. The revised text was first circulated for comment in October 2022. The main amendments include: added new sections on the nature and classification of the pathogen, zoonotic potential and biosafety and biosecurity requirements and differential diagnosis; added the LAMP[10] method to Table 2 *Test methods available for the diagnosis of Marek's disease and their purpose* and amended the rating of the PCR for the purpose *Confirmation of clinical cases* because PCR cannot directly identify MD tumour formation or tumour cells: PCR is not useful for MD diagnosis because MDV including vaccine strains can cause subclinical persistent infection without lymphoma formation; updated the antigen detection section by adding information on immunolabelling techniques, and updated the molecular methods, including the primer and probe sequences; revised Section C and added new sections on validation as a vaccine strain, manufacturing process, duration of immunity and special requirements for recombinant vaccines.

A link to the revised Chapter 3.3.13. *Marek's disease* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

6 IFAT: indirect fluorescent antibody test
7 VN: virus neutralisation
8 MIFI: multiplex fluorometric bead-based immunoassay
9 AGID: agar gel immunodiffusion
10 LAMP: Loop-mediated isothermal amplification

2.13. CHAPTER 3.4.12. LUMPY SKIN DISEASE (DIAGNOSTIC TECHNIQUES SECTION ONLY)

Chapter 3.4.12. *Lumpy skin disease* has undergone a comprehensive revision. The revised text was first circulated for comment in October 2022. The main amendments include: added a paragraph on the findings of phylogenetic analysis of LSDV strains – that the majority of LSDV strains group into two monophyletic clusters – and that recently recombinant LSDV strains have been isolated from clinical cases of LSD in the field, which show unique patterns of accessory gene alleles consisting of sections of both wild-type and "vaccine" LSDV strains; updated the PCR section to include information on quantitative real-time PCR assays that have been designed to differentiate between vaccines and wild-type strains and the limitation of these assays.

A link to the revised Chapter 3.4.12. *Lumpy skin disease* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

A link to the revised Chapter 3.4.12. *Lumpy skin disease* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.14. CHAPTER 3.7.2. RABBIT HAEMORRHAGIC DISEASE

Chapter 3.7.2. *Rabbit haemorrhagic disease* has undergone a minimal revision. The revised text was first circulated for comment in October 2022. The main amendments include: amended Table 1 to remove any conflict between the proposed case definition and the *Terrestrial Manual;* reworded the first paragraph of Section C.3 *Vaccines based on biotechnology*, to improve the clarity of the text.

A link to the revised Chapter 3.7.2. *Rabbit haemorrhagic disease* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.15. CHAPTER 3.9.7. INFLUENZA A VIRUS OF SWINE

Chapter 3.9.7. *Influenza A virus of swine* has undergone a comprehensive revision. The revised text was first circulated for comment in October 2022. The main amendments include: added information on the classification of the H1 virus into clades; in Table 1, amended the rating of virus isolation, the real-time RT-PCR and the ELISA; thoroughly updated most of the diagnostic protocols*,* in particular the RT-PCR and clarified that sequencing is often more precise than real-time RT-PCR for discriminating between subtypes and lineages within a subtype due to the high diversity of swine HA[11] and NA[12] gene sequences; included a new section on gene sequencing; in the vaccine section, expanded the text on the rationale and intended use of the product. In reply to a comment on the use of the term "anthroponosis", the Commission proposed a definition to be added to the glossary of terms

A link to the revised Chapter 3.9.7. *Influenza A virus of swine* is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.

2.16. CHAPTER 3.10.1. BUNYAVIRAL DISEASES OF ANIMALS (EXCLUDING RVF FEVER AND CRIMEAN–CONGO HAEMORRHAGIC FEVER)

Chapter 3.10.1. *Bunyaviral diseases of animals* (*excluding RVF fever and Crimean–Congo haemorrhagic fever*) has undergone a comprehensive revision. The revised text was first circulated for comment in October 2022. The main amendments include: included three completed Table 1 *Test methods available for the diagnosis of* [*pathogenic agent*] *and their*

[11] HA: hemagglutinin
[12] NA: neuraminidase

purpose: for Akabane virus, Schmallenberg virus Nairobi sheep disease (Table 1.1. for of Cache Valley virus is in preparation); added real-time RT-PCR protocols for Schmallenberg virus and Nairobi sheep disease; for Nairobi sheep disease amended the description of virus isolation and added a protocol for VN in cell culture

A link to the revised Chapter 3.10.1. *Bunyaviral diseases of animals* (*excluding RVF fever and Crimean–Congo haemorrhagic fever*) is included on page 1 of the report of the February meeting of the Biological Standards Commission. The revised chapter will be proposed for adoption at the 90th General Session in May 2023.